Clinical Management of Youth with Gender Dysphoria in Vancouver

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Objective To describe patient characteristics at presentation, treatment, and response to treatment in youth with gender dysphoria.

Study design A retrospective chart review of 84 youth with a diagnosis of gender dysphoria seen at BC Children's Hospital from 1998-2011.

Results Of the 84 patients, 45 (54%) identified as female-to-male (FtM), 37 (44%) as male-to-female (MtF), and 2 (2%) as natal males who were undecided. Median age of presentation was 16.9 years (range 11.4-19.8 years) and 16.6 years (range 12.3-22.5 years) for FtM and MtF youth, respectively. Gonadotropin-releasing hormone analog treatment was prescribed in 27 (32%) patients. One FtM patient developed sterile abscesses with leuprolide acetate; he was switched to triptorelin and tolerated this well. Cross-sex hormones were prescribed in 63 of 84 patients (39 FtM vs 24 MtF, $P < .02$). Median age at initiation of testosterone injections in FtM patients was 17.3 years (range 13.7-19.8 years); median age at initiation of estrogen therapy in MtF patients was 17.9 years (range 13.3-22.3 years). Three patients stopped cross-sex hormones temporarily due to psychiatric comorbidities (2 FtM) and distress over androgenic alopecia (1 FtM). No severe complications were noted in patients treated with testosterone or estrogen.

Conclusion Treatment with gonadotropin-releasing hormone analog and/or cross-sex hormones, in collaboration with transgender-competent mental health professionals, is an intervention that appears to be appropriate in carefully selected youth with gender dysphoria. Long-term follow-up studies are needed to determine the safety of these treatments in this age group. *(J Pediatr 2014;164:906-11)*.

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"Transgender" is an umbrella term used to identify individuals whose gender identity does not conform to conventional gender roles of either male or female.[1] More specifically, a transgender female (male-to-female [MtF]) is a natal male who has a gender identity that is female; conversely, a transgender male (female-to-male [FtM]) is a natal female who has a gender identity that is male.[2] The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* has replaced "gender identity disorder" with "gender dysphoria." Gender dysphoria in adolescents and adults (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* 302.85) is defined as "incongruence between one's experienced/expressed gender and assigned gender … causing clinically significant distress and impairment in social, school or other important areas of functioning."[3] Gender dysphoria will often remit in the majority of prepubertal children; however, in most gender dysphoric adolescents, it will not.[4] The prevalence of adolescent-onset gender dysphoria is not known, and there are limited accurate assessments of prevalence of transgenderism in adults in North America. However, the prevalence of adults seeking hormonal or surgical treatment for gender dysphoria is reported to be 1:11 900 to 1:30 400 in the Netherlands.[5] The etiology of gender dysphoria remains poorly understood, but there is increasing evidence of a biologic and/or genetic component.[6-8]

The Amsterdam Gender Identity Clinic developed guidelines and protocols for the diagnosis and clinical management of children and youth with gender dysphoria.[9,10] In pubertal children (ie, having reached Tanner stage 2 or 3) with a confirmed diagnosis of gender dysphoria, pubertal suppression with gonadotropin-releasing hormone analog (GnRHa) therapy is suggested. This is seen as the first step toward transitioning to the perceived gender and allows the patient more time to determine whether a full physical transition is in his or her best interest. Cross-sex hormones (androgens for FtM and estrogens for MtF individuals) are then gradually added to induce the physical changes of the desired gender. This treatment approach is supported by published guidelines from the World Professional Association for Transgender Health[11] and the Endocrine Society[1] related to the diagnosis and treatment of gender dysphoria in children and adolescents.

BCCH	British Columbia Children's Hospital
BCTCCG	British Columbia Transgender Clinical Care Group
FtM	Female-to-male (transgender male)
GnRHa	Gonadotropin-releasing hormone analog
MHP	Mental health professional
MtF	Male-to-female (transgender female)

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The objective of this retrospective study was to describe a Canadian cohort of transgender youth from our program at the Endocrinology and Diabetes Unit at British Columbia Children's Hospital (BCCH) with respect to patient characteristics, clinical management, and response to treatment.

Methods

The BCCH Transgender Program consists of a pediatric endocrinologist, an endocrine nurse clinician, and a social worker who work in partnership with mental health professionals (psychiatrics and psychologists) from the community, allowing for a cohesive "clinic without walls" experience that delivers medical care (ie, GnRHa and cross-sex hormone therapy) and psychosocial support to this population. This medical team was integrated into the British Columbia Transgender Clinical Care Group (BCTCCG) in 2003, with the establishment of resources and written provincial guidelines for transgender youth and adults.[12] Almost all patients are first evaluated by a mental health professional MHP from the BCTCCG who is trained and competent in the diagnosis and management of gender dysphoria in youth. Patients are subsequently referred to the BCCH clinic for medical therapy, usually at the initiation of puberty, as deemed appropriate by the MHP.

Patients included in this study met the following criteria: (1) at least Tanner stage 2 pubertal development (ie, breast development in natal females, testicular enlargement in natal males); (2) previous assessment by an MHP belonging to the BCTCCG; and (3) a confirmed diagnosis of gender dysphoria. All patients underwent a series of psychological tests, including the Utrecht Gender Dysphoria Scale,[13] the Piers-Harris Children's Self Concept Scale,[14] and the Gender Identity Questionnaire for Adolescents,[15] and most were receiving ongoing psychotherapy.

In total, 84 patients seen from January 1998 to December 2011 were included in this study. Of these, 45 natal females identified as male (FtM), 37 natal males identified as female (MtF), and 2 natal males were unsettled in their gender identity. Ethics approval was obtained from the University of British Columbia's Clinical Research Ethics Board.

The following data were obtained from the clinic notes: (1) age at first and most recent visit; (2) age at the start of GnRHa and of cross-sex hormone therapy; (3) natal sex; (4) perceived/affirmed gender; (5) Tanner stage at initial visit (breast for natal females, genital for natal males) and before initiating GnRHa and cross-sex hormones; (6) school grade level at first and most recent visit; and (7) medical and psychiatric comorbidities and complications related to medical treatment(s). Descriptive statistics were used. Data are reported as mean ± SD with 95% CIs and/or as a median and range. Differences between groups were assessed by Fisher exact test or χ^2 test where appropriate. A P value $\leq .05$ was deemed to be significant.

Results

Seventy-eight of the 84 youth (93%) had been assessed by ≥1 MHPs from the BCTCCG (2 psychiatrists and 3 psychologists in different locations in British Columbia) and were diagnosed with gender dysphoria before being seen in our clinic. The remaining 6 patients were seen in our clinic before they had been evaluated by an MHP, but they were not offered cross-sex hormones until they had completed mental health assessment. One of these patients did require therapy with a GnRHa to halt pubertal progression before assessment by an MHP. The median time from assessment by an MHP to the first visit to our clinic was 2.6 months (range 0 months to 7.4 years).

Consistent with other medical care in British Columbia, the majority of patients (68%) were referred to our clinic by their family physician or a walk-in clinic after being assessed by a psychologist; 25% were referred directly by a psychiatrist; and 7% were referred by a pediatrician or other subspecialist. The patient referral pattern roughly represented the geographical distribution of the province; only 1 patient was from out of province. The number of new referrals for gender dysphoria from 1998 to 2011 is shown in the Figure.

Initial Clinical Presentation

The characteristics of our patient population are summarized in Table I. Two MtF patients had disorders of sex development (Klinefelter syndrome and mild partial androgen insensitivity syndrome). At the first clinic visit, most patients were in school grades 8-10 (32%) or grades 11-12 (48%); 12% were in grades 5-7, and the remaining 8% were in college/university or no longer attending school.

GnRHa Treatment Approach

The median time between the first visit to our clinic and initiation of GnRHa was 0.2 month (range 0-3.2 months), with 12 of 27 patients (44%) receiving treatment at their first visit to our clinic. Of the 15 FtM patients receiving GnRHa, 14 transitioned to testosterone treatment during the observation period. Seven of these patients continued on GnRHa after starting testosterone; the other 7 patients discontinued GnRHa (after a median of 3.0 years, range 0.2-9.2 years). Five of the latter discontinued GnRHa at the time of hysterectomy and salpingo-oophorectomy, 1 discontinued GnRHa

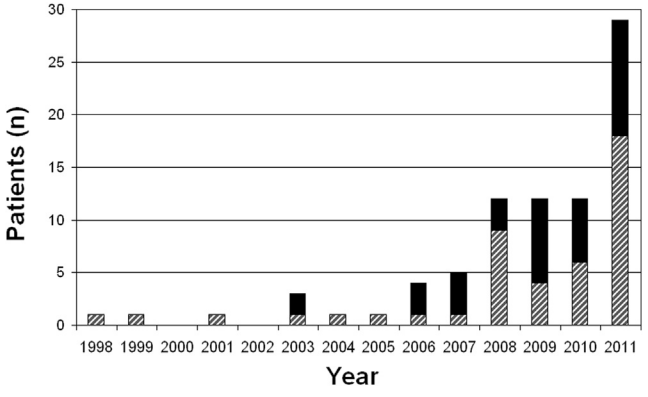

Figure. Number of new patients with gender dysphoria seen in 1998-2011. MtF, *black bars*; FtM, *hatched rectangles*.

Table I. Clinical characteristics of patients with gender dysphoria

Characteristics	All (n = 84)	FtM (n = 45)	MtF (n = 37)
Age at first visit, yr			
Mean ± SD (95% CI)	16.6 ± 2.2 (16.1-17.0)	16.4 ± 2.1 (15.8-17.0)	16.8 ± 2.4 (16.0-17.5)
Median (range)	16.8 (11.4-22.5)	16.9 (11.4-19.8)	16.6 (12.3-22.5)
Age at most recent visit, yr			
Mean ± SD (95% CI)	18.2 ± 2.3 (17.7-18.7)	18.4 ± 2.2 (17.7-19.0)	18.2 ± 2.5 (17.4-19.0)
Median (range)	18.2 (12.5-24.5)	18.3 (13.8-24.5)	18.1 (12.5-23.5)
Follow-up time,* n (%)	61 (73)	33 (73)	26 (70)
Mean ± SD (95% CI), y	2.3 ± 2.1 (1.8-2.8)	2.6 ± 2.5 (1.8-3.5)	2.0 ± 1.4 (1.5-2.5)
Median (range), y	2.0 (0.0-11.3)	2.2 (0.0-11.3)	2.0 (0.3-5.1)
Age at start of GnRHa treatment,† n (%)	27 (32)	15 (33)	11 (30)
Mean ± SD (95% CI), y	14.7 ±1.9 (14.0-15.4)	14.8 ± 2.1 (13.7-15.9)	14.7 ± 1.7 (13.6-15.7)
Median (range), y	14.4 (11.4-17.9)	14.3 (11.4-17.9)	14.8 (12.3-17.9)
Tanner stage at start of GnRHa treatment			
2-3, n (%)	10 (37)	4 (27)	5 (45)
4-5, n (%)	16 (59)	10 (67)	6 (55)
Age at start of cross-sex hormones, n (%)	63 (75)	39 (87)	24 (65)
Mean ± SD (95% CI), y	17.4 ± 1.9 (16.9-17.9)	17.0 ± 1.6 (16.5-17.5)	14.7 ± 2.2 (13.8-15.5)
Median (range), y	17.5 (13.3-22.2)	17.3 (13.7-19.8)	17.9 (13.3-22.3)
Tanner stage at start of cross-sex hormones			
2-3, n (%)	7 (11)	6 (15)	1 (4)
4-5, n (%)	53 (84)	32 (82)	21 (88)
Age at start of spironolactone,‡ n (%)	N/A	N/A	25 (68)
Mean ± SD (95% CI), yr	N/A	N/A	17.6 ± 1.9 (16.9-18.3)
Median (range), yr	N/A	N/A	17.5 (15.0-22.0)
Tanner stage at start of spironolactone			
2-3, n (%)	N/A	N/A	0
4-5, n (%)	N/A	N/A	25 (100)

*Patients with >1 visit in clinic.
†One natal male undecided on GnRHa and 1 FtM was started GnRHa by another physician and Tanner stage not included.
‡One natal male undecided started on spironolactone.

(after 2.2 years) at the time of transitioning to cross-sex hormones, and 1 patient was on GnRHa for <2 months and chose to stop treatment due to mood swings and emotional lability.

Of the 11 MtF patients, 5 received estrogen treatment during the observation period; of these, GnRHa was discontinued in only 1 of these patients at that time. Of the remaining 6 MtF patients receiving GnRHa, 1 stopped GnRHa after a few months due to emotional lability. Another patient stopped GnRHa as well; although she met hormone-readiness criteria, cross-sex hormones were withheld because of continued heavy tobacco smoking. She was prescribed estrogen the following year, once there was a substantial decrease in tobacco use. One natal male with undecided gender was prescribed GnRHa, but he discontinued this after 13 months, as he chose not to pursue transition.

GnRHa Treatment Side Effects

Of the 27 patients treated with GnRHa, 1 FtM patient developed sterile abscesses; he was switched from leuprolide acetate to triptorelin, and this was well tolerated. One FtM patient developed leg pains and headaches on GnRHa, which eventually resolved without treatment. Another patient gained 19 kg within 9 months of initiating GnRHa, although the patient's body mass index was >85 percentile before initiation of GnRHa.

Antiandrogen Treatment Approach

Any MtF patient choosing not to take GnRHa was offered treatment with the antiandrogen spironolactone, to lessen androgen-dependent hair growth. Twenty-five of 37 (68%) FtM patients chose this therapy. All patients on spironolactone had electrolyte and urea/creatinine levels checked when they were on full dose; there were no abnormalities noted.

Cross-Sex Hormone Treatment Approach

In total, 63 of 84 patients (75%) were treated with cross-sex hormones during the observation period, with a significantly

Table II. Psychiatric comorbidities

Psychiatric comorbidities*	All (n = 84) n (%)	FtM (n = 45) n (%)	MtF (n = 37) n (%)	P‡
ADHD	8 (10)	2 (4)	6 (16)	NS
Mood disorder	29 (35)	20 (44)	7 (19)	.01
Anxiety disorder	20 (24)	15 (33)	4 (11)	.02
Eating disorder	4 (5)	2 (4)	2 (5)	NS
PDD/ASD	6 (7)	2 (4)	4 (11)	NS
≥2 DSM-IV diagnoses	22 (26)	12 (27)	9 (24)	NS
Substance abuse†	6 (7)	2 (4)	4 (11)	NS
Suicide attempt/ED visit				NS
Before first visit to our clinic	10 (12)	6 (13)	2 (5)	
After first visit to our clinic	4 (5)	3 (7)	1 (3)	
Psychiatric hospitalization§				NS
Before first visit to our clinic	10 (12)	7 (16)	3 (8)	
After first visit to our clinic	1 (1)	1 (2)	-	

ADHD, attention-deficit/hyperactivity disorder; *DSM-IV*, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; *ED*, emergency department; *NS*, nonsignificant; *PDD/ASD*, pervasive developmental disorder/autism spectrum disorder.
*Diagnosis made by an MHP (psychiatrist or psychologist). Other diagnoses include 1 patient with trichotillomania, 2 with borderline personality disorder, 1 with psychosis not otherwise specified, 1 with adjustment disorder, 2 with tic disorders, and 1 with oppositional-defiant disorder.
†Cannabis dependence, polysubstance abuse.
‡Fisher exact test or χ^2 test, $P < .05$ significant.
§Conditions requiring hospitalization include posttraumatic stress disorder, depression, substance abuse, behavioral issues, psychosis, and anxiety.

larger proportion of FtM patients (39/45, 87%) than MtF patients (24/37, 65%) treated ($P < .02$). Of these, 40 patients (64%) had 1 or 2 parents sign an informed consent form for cross-sex hormones. Under the British Columbia Infants Act, any child of any age can consent to a medical treatment, provided that he or she can demonstrate the capacity to understand the risks and benefits of treatment. Fifteen of 63 patients (24%) received cross-sex hormone treatment at their first visit to our clinic. The median time from first visit to start of cross-sex hormones was 4.6 months (range 0-42 months). Of the 19 patients who transitioned from GnRHa to cross-sex hormones, the median time from start of GnRHa to the start of cross-sex hormones was 11.3 months (range 2.2-42 months). Injectable testosterone enanthate and/or cypionate was used for the FtM patients, and oral micronized 17β-estradiol was used for the MtF patients. Our treatment protocol for hormonal therapy is based on the guidelines published by the Endocrine Society.[1] All patients receiving cross-sex hormones had routine hematologic, biochemic, and sex-hormone testing performed when they were on near-adult doses and then annually.

Cross-Sex Hormone Treatment Side Effects

Twelve of 37 FtM patients (32%) treated with testosterone developed minor, expected complications: 7 developed severe acne necessitating isotretinoin treatment, 1 developed early-onset (age <20 years) androgenic alopecia, 3 developed mild dyslipidemia, and 1 patient had significant mood swings. No severe complications, such as erythrocytosis or severe liver dysfunction, were noted with testosterone use, and no minor or severe complications, such as thromboembolic disease or severe liver dysfunction, were noted with estrogen use.

None of the 63 patients receiving cross-sex hormones discontinued his or her treatment permanently. Three of the 37 FtM patients temporarily stopped treatment: 2 due to concomitant psychiatric comorbidities (an eating disorder in one patient and depression in another), and 1 patient stopped treatment due to distress over androgenic alopecia; they all eventually resume treatment. There were no interruptions in treatment with cross-sex hormones in the MtF patients prescribed estrogen.

Surgical Outcomes

Seven of 37 MtF patients (19%) attempted semen cryopreservation (all Tanner 5) before starting estrogen. Nine of 42 FtM patients (21%) underwent mastectomy with male chest contouring (median age 18.1 years, range 14.9-22.1 years) during the observation period. Of these 9 patients, 6 proceeded to hysterectomy and salpingo-oophorectomy (median age 18.9 years, range 16.5-22.3 years). One patient underwent hysterectomy and salpingo-oophorectomy but did not require chest surgery, as the patient was treated with GnRHa early and had negligible breast growth. One MtF patient underwent elective breast-augmentation surgery and tracheal shaving. Two MtF patients underwent penectomy, orchidectomy, and vaginoplasty (at 18 and 21 years of age) during the observation period.

Psychiatric Comorbidity

Psychiatric comorbidities are presented in Table II. Mood and anxiety disorders were more common in FtM than in MtF patients (44% vs 19%, $P = .01$, and 33% vs 11%, $P = .02$, respectively). Importantly, 10 of the 84 patients (12%) had attempted suicide with a resultant visit to an emergency department before being seen in our clinic vs 4 (5%) after their first visit.

Discussion

Our results indicate an increase in the number of patients over the past few years, also described at other pediatric centers.[16] Potential reasons for this increase include more media attention on this topic and/or more adolescents "coming out" at an earlier age as transgender.[16] In the past 10 years, the publication of guidelines for health care professionals, presentations on endocrine management of transgender youth at international conferences, and, in our province, the successful development of the BCTCCG with increased physician awareness of this issue are likely significant contributing factors to the increase in referrals. We also did see a number of 18- to 20-year-old patients during a period of limited access to care in the adult system.

Despite increased public awareness, many clinicians continue to be reluctant to prescribe GnRHa, even though this treatment is strongly recommended as an appropriate intervention for adolescents with gender dysphoria.[10] Our results are encouraging, with only 1 of the 27 patients treated with GnRHa deciding to stop treatment due to emotional lability, and not because of unwillingness to pursue transition.

Fewer patients in our cohort (32%), compared with 79% of the Dutch cohort of transgender youth, were treated with GnRHa. Antiandrogens are not prescribed for transgender youth in the Netherlands, as most individuals are treated with GnRHa; in our cohort, most MtF individuals were treated with antiandrogens. The cost of monthly therapy ($425 CDN per 7.5-mg kit) likely was not an issue, as GnRHa treatment is covered by our provincial drug plan, subject to income-dependent deductibles and co-pays, and in general every patient who desired GnRHa was able to receive it with full or partial insurance coverage. As well, many older patients elected to defer GnRHa therapy and wait for cross-sex hormone therapy.

Most experts in transgender care would agree that initiation of GnRHa therapy at an earlier stage of puberty is preferred,[17] because preventing the development of unwanted secondary sexual characteristics can alleviate distress. Many MtF patients who take GnRHa or antiandrogens before the development of significant androgen-dependent hair are spared the need for electrolysis. This approach also leads to better surgical outcomes, as FtM patients treated early with GnRHa who undergo mastectomy have a more favorable postoperative

appearance; some early-treated FtM patients may not require such surgery at all.

It is now standard practice to discuss fertility preservation with adolescents before initiating medical or surgical treatments. For some MtF patients, it may be more appropriate to introduce GnRHa therapy at a later pubertal stage, to allow the patient the option of semen cryopreservation to maintain fertility. A study investigating the opinions of 121 transgender women (MtF) by Internet-based survey found that 51% of the study group (n = 61) would have seriously considered sperm banking or would have actually done so if this had been offered to them.[17] We therefore recommend that all adolescents identified as MtF be asked about their desire for biological children and that the option of sperm banking be discussed.

As techniques for oocyte preservation continue to be developed and improved, it will also be important to counsel FtM patients about this option before beginning medical or surgical treatment.

A second issue arises in MtF individuals who receive GnRHa at the early stages of puberty. Adolescents with male genitalia who transition may be adversely affected by early initiation of GnRHa therapy, because this might result in insufficient genital tissue for the common surgical technique of penile inversion vaginoplasty.

Significant psychiatric comorbidities have been described in transgender youth. Our cohort had a greater proportion of patients with mood disorders compared with a Dutch cohort (35% vs 12%); however, the frequency of anxiety disorders was similar (24% and 21%, respectively).[18] As noted in the Dutch cohort, it can be problematic to compare frequency of psychiatric comorbidity in adolescents with gender dysphoria across clinics, as the same diagnostic criteria or measures may not be used.[18] The older age of our cohort of patients compared with the Dutch cohort (mean age 16.6 vs 14.6 years, respectively) may also explain differences in frequency of psychiatric comorbidity, as our patients had more time to develop these comorbidities.

Suicidal ideation and suicide attempts are also concerns among transgender youth. In 1 cross-sectional study of 55 adolescents, 45% reported to have seriously contemplated suicide,[19] and in another cohort study of 97 patients, 9.3% had attempted suicide.[20] In our study, suicide attempts and/or emergency department visits for suicidal ideation decreased from 12% (n = 10) before the first visit to our transgender clinic to 5% (n = 4) afterward. Although our numbers are quite small, this finding suggests a lessening of emotional problems and suicidality when puberty blockers or cross-sex hormones are started. This is further corroborated by findings in the Dutch cohort, where an improvement in psychological functioning in areas such as depressive symptoms was demonstrated in adolescents with gender dysphoria treated with GnRHa for nearly 2 years.[4,10]

There are some limitations to this study. This was a retrospective review with a small absolute number of patients. However, adolescent gender dysphoria is a rare condition, and there is a paucity of studies in this group. We did have a short follow-up time and therefore cannot comment on the long-term safety of GnRHa and cross-sex hormone therapy. Lastly, objective tests of psychological functioning before and after treatment were not performed systematically; these would have been helpful in better assessing the benefits of initiating GnRHa and cross-sex hormone therapy at this earlier age. ■

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References

1. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, Gooren LJ, Meyer WJ III, Spack NP, et al. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2009;94:3132-54.
2. Olson J, Forbes C, Belzer M. Management of the transgender adolescent. Arch Pediatr Adolesc Med 2011;165:171-6.
3. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed., text revision (DSM-V). Washington, DC: American Psychiatric Association; 2013.
4. de Vries AL, Steensma TD, Doreleijers TA, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. J Sex Med 2011;8:2276-83.
5. van Kesteren PJ, Gooren LJ, Megens JA. An epidemiological and demographic study of transsexuals in The Netherlands. Arch Sex Behav 1996; 25:589-600.
6. Zhou JN, Hofman MA, Gooren LJ, Swaab DF. A sex difference in the human brain and its relation to transsexuality. Nature 1995;378: 68-70.
7. Hare L, Bernard P, Sánchez FJ, Baird PN, Vilain E, Kennedy T, et al. Androgen receptor repeat length polymorphism associated with male-to-female transsexualism. Biol Psychiatry 2009;65:93-6.
8. Ujike H, Otani K, Nakatsuka M, Ishii K, Sasaki A, Oishi T, et al. Association study of gender identity disorder and sex hormone-related genes. Prog Neuropsychopharmacol Biol Psychiatry 2009;33:1241-4.
9. de Vries AL, Cohen-Kettenis PT. Clinical management of gender dysphoria in children and adolescents: the Dutch approach. J Homosex 2012;59:301-20.
10. Kreukels BP, Cohen-Kettenis PT. Puberty suppression in gender identity disorder: the Amsterdam experience. Nat Rev Endocrinol 2011;7: 466-72.
11. The World Professional Association for Transgender Health. Standards of care for the health of transsexual, transgender, and gender nonconforming people, 7th version. 2011. http://www.wpath.org/. Accessed November 20, 2013.
12. Transgender Health Program. De Vries ALC, Cohen-Kettenis PT, Delemarre-Van de Wall H. Caring for transgender adolescents in BC: suggested guidelines 2006. http://transhealth.vch.ca/resources/library/. Accessed June 24, 2013.
13. Cohen-Kettenis PT, van Goozen SH. Sex reassignment of adolescent transsexuals: a follow-up study. J Am Acad Child Adolesc Psychiatry 1997;36:263-71.

14. Piers EV, Harris DB, Herzberg DS. Piers-Harris self concept scale. Los Angeles, CA: Western Psychological Services; 2001.
15. Deogracias JJ, Johnson LL, Meyer-Bahlburg HF, Kessler SJ, Schober JM, Zucker KJ. The gender identity/gender dysphoria questionnaire for adolescents and adults. J Sex Res 2007;44:370-9.
16. Zucker KJ, Bradley SJ, Owen-Anderson A, Kibblewhite SJ, Cantor JM. Is gender identity disorder in adolescents coming out of the closet? J Sex Marital Ther 2008;34:287-90.
17. De Sutter P, Kira K, Verschoor A, Hotimsky A. The desire to have children and the preservation of fertility in transsexual women: a survey. 2002. http://www.iiav.nl/ezines/web/ijt/97-03/numbers/symposion/ijtvo06no03_02.htm. Accessed November 20, 2013.
18. de Vries AL, Doreleijers TA, Steensma TD, Cohen-Kettenis PT. Psychiatric comorbidity in gender dysphoric adolescents. J Child Psychol Psychiatry 2011;52:1195-202.
19. Grossman AH, D'Augelli AR. Transgender youth and life-threatening behaviors. Suicide Life Threat Behav 2007;37:527-37.
20. Spack NP, Edwards-Leeper L, Feldman HA, Leibowitz S, Mandel F, Diamond DA, et al. Children and adolescents with gender identity disorder referred to a pediatric medical center. Pediatrics 2012;129:418-25.